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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/012,846	01/23/98	CHARETTE M	CRP-141

HM12/0902

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EXAMINER	
WEATHERSPOON, J	
ART UNIT	**PAPER NUMBER**
1645	5

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/012,846	Applicant(s) Charette
	Examiner John K. Weatherspoon	Group Art Unit 1645

☒ Responsive to communication(s) filed on *Jan 23, 1998* .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-26* is/are pending in the application.

Of the above, claim(s) *23-26* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-22* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-22, drawn to compositions comprising a morphogen, and methods for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal tissue damage in a mammal comprising administering to mammal a morphogen, classified in class 424, subclass 9.2.

II. Claims 1-10 and 25, drawn to composition comprising a nucleic acid encoding a morphogen, and methods for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal tissue damage in a mammal comprising administering to mammal a nucleic acid encoding a morphogen, classified in class 514, subclass 44.

III. Claims 23, 24 and 26, drawn to compositions comprising cultured cells competent to express a morphogen, a kit comprising cells competent to express morphogen, and a receptacle for said cells, classified in class 435, subclass 325.

2. The inventions are distinct, each from the other because of the following reasons:

The claims of Groups I and II are drawn to distinct methods which differ in the method objectives, steps and parameters. Group I contains claims drawn to methods for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal tissue damage in a mammal, comprising administering to mammal

a morphogen. Group II contains claims drawn to methods for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal tissue damage in a mammal comprising administering to mammal a nucleic acid encoding a morphogen. Since morphogen and nucleic acid encoding a morphogen are structurally and functionally distinct, i.e. nucleic acid comprises nucleotides and functions to encode morphogen, in contrast to morphogen which comprises amino acids and does not encode morphogen, thus methods comprising administering to mammal said morphogen and administering to mammal said nucleic acid encoding a morphogen are clearly distinct.

The claims of Groups I-III are drawn to structurally and functionally distinct products. Group I contains claims drawn to compositions comprising a morphogen. Group II contains claims drawn to composition comprising a nucleic acid encoding a morphogen. Group III contains claims drawn to compositions comprising cultured cells competent to express a morphogen, a kit comprising cells competent to express morphogen, and a receptacle for said cells, classified in class 435, subclass 325. Morphogen of Group I and nucleic acid encoding a morphogen of Group II are structurally and functionally distinct, i.e. nucleic acid comprises nucleotides and functions to encode morphogen, in contrast to morphogen which comprises amino acids and does not encode morphogen. Further, said cultured cells of Group III are structurally and functionally distinct from said morphogen and nucleic acid encoding a morphogen, since said cultured cells comprise cellular components (e.g. lipid bilayer, ribosomes, etc) that are not present in the products of Groups I and II. These products are clearly distinct.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classifications and/or recognized divergent subject matter and because the searches required for examination of the groups identified above are not coextensive, restriction for examination purposes as indicated is proper.

During a telephone conversation with Thomas Meyers on June 8, 1999, a provisional election was made with traverse to prosecute the invention of Group I, claims 1-22. Affirmation of this election must be made by applicant in replying to this Office action. Claims 23-26 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Information Disclosure Statement

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be

incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Drawings

4. This application has been filed with informal drawings which are acceptable for examination purposes only. The drawings are objected to by the draftsperson under 37 C.F.R. 1.84 or 1.152. See PTO-948 for details. Correction of the noted defects can be deferred until the application is allowed by the examiner.

Claim Rejections - 35 USC § 112 first paragraph

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant specification provides insufficient guidance for claimed methods for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal damage in a mammal comprising adminstering to mammal any morphogen as broadly claimed, for the reasons discussed below.

The specification provides insufficient guidance on how to successfully practice the full scope of the invention, as currently claimed, because it is further unknown what metes and bounds are envisioned by the claimed recitations drawn to "treating", i.e. "treating dementia" and "treating a symptom associated with hippocampal tissue damage" in a mammal, and by the recitations "protecting cognitive function" and "reducing memory dysfunction", because no *in vivo* models are known, or adequately described, by which one skilled in the art could extrapolate "how to use" the invention with any reasonable expectation of success, for the reasons indicated below. It is well accepted in the art the differences exist between *in vitro* protocols and results, versus *in vivo* protocols and results, especially as it relates to undefined parameters that do not distinguish when "treating" is effective, or that require passage across the blood brain barrier which is impermeable to protein molecules/other molecules, or that involve undefined parameters that do not distinguish "treating" of "dementia", for example, from any different disease state. The instant specification provides insufficient guidance on how these parameters are to be determined, how a similar method was practiced in the art with a different agent or to provide even a single working *in vivo* example of the claimed methods. Additionally, it is not known to one skilled in the art at what point during any given disease state of "dementia" or state of "cognitive function" or "memory dysfunction" exactly when claimed methods are recommended, or how one skilled in the art knows when, or if, they have successfully practiced the instant invention; thereby, requiring undue experimentation to discover how to successfully practice applicants' invention. Further, it is unknown, nor disclosed, what specific

aspects/symptoms of these claimed neurological disorders (e.g. amnesia, Alzheimer's Disease, "brain tissue damage" as claimed) are envisioned to be "treated" or what constitutes a therapeutically effective amount of the structurally deficient/uncharacterized morphogens claimed, or how to assay such *in vivo*. One skilled in the art would not reasonably be able to successfully make and use the claimed invention absent undue experimentation.

Further, the state of the art is unpredictable with regard to *in vivo* methods i.e. in mammals as claimed) since, in particular, neurons do not regenerate in the CNS, e.g. in response to the methods (i.e. in mammals as claimed) comprising administering claimed morphogens (see page 305, last paragraph, of Jackowski; cited on PTO-892). Jackowski teaches that without functional synaptogenesis, there is no functional regeneration; therefore, no regeneration, repair or preservation of any neural pathway that is the result of a neurological disease state that results in loss of synaptic (i.e., including dendritic) contacts, and subsequent neuronal cell death. Applicants specification provides insufficient guidance on how to enable the full scope of the claimed methods comprising administering claimed morphogens; nor how any of the unique disorders recited in the claims, each with their unique etiology, can be ameliorated, especially within the CNS. Moreover, the instant specification discloses no assay that enables one skilled in the art to determine whether the applicants invention works in "treating" as claimed in this unpredictable art. Further, no assays are disclosed in the specification that allow one skilled in the art to extrapolate what critical amino acids constitute the tissue-specific morphogenic function for practicing the claimed invention. Further, the specification provides insufficient

guidance that would be needed by a routine practitioner to administer any morphogen, such as OP-1 to the CNS, because these proteins do not readily cross the blood brain barrier. In the absence of this guidance a practitioner would have to resort to undue experimentation involving the variation in the amount and duration of administration of any morphogens as claimed of the instant invention and in determining a suitable route of administration, because no appropriate assay is disclosed to determine when, or if, the instant invention works for neural-specific systems. *In vitro* induction of N-CAM and L1 in NG-108 cultures, clearly can not be reasonably extrapolated to an appropriate assay to determine putative effects on neuronal populations; especially *in vivo* for the reasons set forth above.

Further, applicants specification provides insufficient guidance on how to enable the full scope of the claims associated with protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal damage in *any* mammal as broadly claimed. In other words, the specification provides insufficient guidance on how to exactly assess "cognitive function", "memory dysfunction" and "dementia" in *any* mammal in view of the teachings of Smith (below), and thus it would require undue experimentation for one skilled in the art to determine when one has successfully practiced the methods of the claimed invention, considering the heterogeneity of neural systems underlying such processes in mammals, as taught by Smith (below). For example, Smith teaches that not all mammals possess the same neural processes that underly memory, e.g. "the upshot is the vastly increased range and subtlety of the memory process in the higher animals. In the case of Homo sapiens, of course, the

situation is complicated yet further by the development of symbolic representation and communication-language" (see Smith, entire reference; cited on PTO-892). Thus, absent sufficient guidance from the instant specification with regard to practicing the claimed invention in any mammal, given the heterogeneity of neural sytems among mammals, one skilled in the art would require undue experimentation to practice the invention as broadly claimed.

Further, in view that one skilled in the art recognizes cognitive function, memory dysfunction, dementia, and symptoms associated with hippocampal tissue damage are elements/characteristics that involve complex neuronal pathways (see Smith et al; cited on PTO-892), and further that neuronal tissue does not possess tumorigenic properties, unlike NG108-15 cells as claimed, the specification provides insufficient guidance with regards to exactly how NG108-15 cells are involved with/relevant to cognitive function, memory dysfunction, dementia, and symptoms associated with hippocampal tissue damage. Further, the specification provides insufficient guidance with regards to exactly how stimulation of "production of an N-CAM or L1 isoform by an NG108-15 cell in vitro" by claimed morphogens is requisite/necessary for claimed methods for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal tissue damage in a mammal. Further, N-CAM is not representative of any other distinct neural adhesion molecule; nor is N-CAM gene expression reasonably expected to be the same as differently regulated neural adhesion molecules, each with their own unique regulatory promoter sequences; nor can OP-1 induction of N-CAM in tumor cell lines be extrapolated to administering any "morphogen", or provide any basis for *in vivo*

administration of proteins which do not cross the blood brain barrier due to the presence of tight junctions, as taught by Smith et al (see pages 141-142 of Smith reference; see entire document). One skilled in the art recognizes that OP-1 is but one protein which alone is not reasonably extrapolated to all "generic" proteins containing seven cysteines, and that N-CAM is but one neural adhesion molecule, whose activity is not extrapolated to any other different neural adhesion molecule. The limited guidance provided by the specification clearly would not allow one skilled in the art to know how to successfully practice the instant invention without undue experimentation to discover how to make and use applicants' invention, as broadly claimed. The instant specification discloses no assay on how to access when, or if, applicants' invention works for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal tissue damage in a mammal *in vivo* that is commensurate in scope with that claimed.

Further, one skilled in the art recognizes that stimulation of an N-CAM or L1 isoform by culturing of *non-neuronal tumorigenic* cells *in vitro* provides no nexus for extrapolating to effective *in vivo* treatment of mammalian nervous system cells/ pathways, or to effective methods for treating dementia, treating a symptom associated with hippocampal tissue damage, protecting cognitive function, or reducing memory dysfunction as claimed, because no neural pathways are present in cell cultures; and because of the unpredictability within the art as to what neuronal cell populations are putatively responsive to OP-1; and because neuronal tissue does not possess tumorigenic properties, unlike NG108-15 cells; and because it is unknown nor disclosed what

phenotypes could or would be assayed, so that the skilled artisan knows when, or if, the instant invention works, as previously made of record. Clearly one skilled in the art would not reasonably expect the instant invention to successfully work *in vivo* without undue experimentation to discover how to use applicants' invention, for the above reasons, and because the limited guidance provided from the specification constitutes merely an invitation to experiment to discover how to make and use applicants' invention; thereby, being not enabled. Further, one skilled in the art would predict that only specific, yet unknown and undisclosed, populations of neuronal cells would reasonably be responsive to OP-1; that only N-CAM and L1 are described, or known, to be expressed or active in the nervous system; that because these proteins do not readily cross the blood brain barrier and because the specification provides insufficient guidance to disclose how these parameters are to be determined for effective administration to practice the claimed methods, how a similar method was practiced in the art with a different agent, or to provide even a single working *in vivo* example of the claimed methods, it would require undue experimentation for one skilled in the art to determine such.

Further, in view that the claimed invention is drawn to methods for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal damage in a mammal comprising administering to any mammal any morphogen as broadly claimed, including wherein said morphogen has "at least 70% homology/ greater than 60% amino acid sequence identity...with the C-terminal seven-cysteine skeleton of human OP-1" which encompasses claimed morphogens with amino acid substitutions, deletions,

insertions and/or additions, one skilled in the art recognizes that undue experimentation would be required to practice the invention as claimed, given that the biological function of claimed morphogens (i.e. by amino acid substitutions, deletions, insertions and/or additions) is unpredictable, in view of the teachings discussed below. Burgess and Lazar (see below) teach that protein chemistry is probably one of the most unpredictable areas of biotechnology (see below) and that even a single amino acid substitution can alter biological function in an unpredictabel manner. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological activity of the protein (see Burgess et al.). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduce the biological activity of the mitogen (see Lazar et al.). These references teach that the function of particular amino acids of a molecule with regard to biological function, for example biological function of claimed morphogens with regard to protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal damage in a mammal, upon amino acid substitutions, deletions, insertions and/or additions of amino acid sequence said morphogens, is unpredictable *a priori* and thus one skilled in the art would be forced into undue experimentation in order to practice broadly the claimed invention. These teachings indicate that the biological function of amino acid substitution variants is unpredictable with regard to the methods claimed. In view of the lack of guidance, lack of examples, and lack

of predictability associated with regard to producing and using the myriad of derivatives and fragments encompassed in the scope of the claims, one skilled in the art would be forced into undue experimentation in order to practice broadly the claimed invention. The specification does not support the broad scope of the claims which encompass a multitude of analogs or equivalents because the specification does not disclose specific positions which can be predictably modified, and provides essentially no guidance to which of the enormous possible choices of peptides is likely to be successful. Thus, applicants have not provided sufficient guidance to enable one skilled in the art to make and use the claimed derivatives in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without such guidance, the changes which can be made and still maintain activity/utility is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See Ex parte Forman, 230 U.S.P.Q. 546 (Bd. Pat. App. & Int. 1986).

Further, one skilled in the art recognizes that the instant specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims in view of the teachings discussed below. Lein et al (see PTO-892; see abstract, pg. 597, and entire reference) teach that "OP-1 requires NGF as a co-factor...in optimal concentrations". Lines 23-25 in the 2nd column of Lein (pg. 597) then teach that "[I]ndeed, the only trophic factor that has been clearly implicated in the regulation of the initial stages of dendritic growth is nerve growth factor

(NGF)." In other words, without NGF there is no neurite outgrowth/synaptic contact. Without OP-1 there is still outgrowth in culture, therefore OP-1 is inert. Varley et al teach that "OP-1 does not act on a postmitotic cell population" (see pgs. 441-442). Therefore, because neurons, by definition, are postmitotic/amitotic after birth, this reference clearly establishes that the instant invention can not work *in vivo* in a mammal without undue experimentation to determine otherwise; thereby, not being enabled. Wilson et al (see PTO-892) disclose that BMPs as broadly claimed do not predictably enhance "preserving/ restoring" synaptic contacts because, conversely, BMP-4 is a "neural inhibitor" (e.g., pg. 331, Abstract). Withers et al (see PTO-892) state that "no synaptic contacts were observed", which is the result of "two possibilities: 1) the OP-1 [i.e, the preferred embodiment of the instant invention] induced dendrites were not receptive to innervation; or 2) the poor growth of axons in these cultures prevented normal synaptic contacts from occurring". In other words, *in vitro* culturing of NG108-15 cells provides no nexus for how to administer a putative protein that may or may not affect neurons *in vivo*; nor how to assess when, *or if*, the invention works *in vivo*; especially when insufficient guidance is provided by the specification to extrapolate to such treatment. The teaching of Withers et al indicates to one skilled in the art that the claimed invention cannot be predicted to work *in vitro*, and by analogy does is not predicted to work *in vivo,* without undue experimentation to determine otherwise. Jackowski (see PTO-892) teaches that CNS neurons do not regenerate (pg 305, last *pp).* In other words, because the minimal requirement for restoring/preserving synaptic contacts required for protecting cognitive function, reducing memory dysfunction, treating

dementia, and treating a symptom associated with hippocampal tissue damage is that *de novo* axonal cell growth be completed for a sufficient distance to re-establish a proximity relationship to the prior target, no reasonable expectation of success is accepted in the art. It is noted that neuropathy/spinal cord injury, by definition, lose synaptic contacts and degenerate due to normal Wallerian degeneration (e.g., see Jackowski, pg. 304). Accordingly, regeneration/restoration of synaptic contacts/motor function does not occur either because processes fail to grow the necessary distance, they are in competition with other nearby neuronal processes not derived from the affected nerve, scarring blocks axonal elongation, or because of misdirected axonal growth (e.g., see Jackowski, pgs. 309-310).

Further, one skilled in the art recognizes that the instant specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims since dead neurons characterize "neurodegenerative disorders" as claimed, such as ALS or spinal cord injury. Therefore, restoring or preserving motor function does not occur, as claimed. Thus, the claims are not commensurate in scope with that disclosed within the specification for treating neurodegenerative disorders, in general, and as such, merely constitutes an invitation to experiment to discover if Applicants' invention works *in vivo*. Further, the non-neuronal tumor cell line, NG108-15, is not neuronal tissue, nor amitotic neurons, nor representative of any *in vivo* nervous system tissue. Nor are any appropriate neuro-specific assays provided in the instant specification to distinguish those putative "morphogens" from different proteins which do not

have the desired activity of the instant invention, as it relates to affecting any neuronal populations; especially *in vivo*. Further, i*n vitro* tissue culture of non-neuronal tumorigenic cells provides no nexus to extrapolating to effective *in vivo* treatment of mammals, because no neural pathway are present in cell cultures, NG108 cells do not die, and these tumorigenic cells continue to proliferate, unlike neurons. Further, stimulation of N-CAM or L1 production is not equivalent to "treating" as claimed.

Further, the name "morphogen" as it relates to the generic sequences claimed, or to the recitation of the name alone, sets forth little or no structural characteristics, and little functional characterization. The specification does not teach which specific amino acids are critical for any morphogen function, nor how to distinguish such from any different polypeptide sequences that possess none of the desired functions of the instant invention, yet are encompassed by the claims. For example, cysteines alone would not be expected to possess any desired biological activity (i.e., as it relates to the generic sequences recited). Moreover, random mutations, substitutions, insertions, deletions, or biologically functional equivalents of different morphogen molecules would be expected by the skilled artisan to conversely result in proteins with unpredictable function or inactive proteins (see discussion above). The lack of guidance provided in the specification, as to what minimal structural requirements are necessary for determining how to make and use any biologically functional equivalent morphogen in the proposed method of the instant invention, would prevent the skilled artisan from determining when they are in possession of the necessary components for practicing the invention, because random mutations of any

protein would be expected by the skilled artisan to adversely affect the three-dimensional conformation of these molecules, without undue experimentation to determine otherwise.

Claim Rejections - 35 USC § 112 second paragraph

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15-22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The terms "70% homology" and "60% amino acid sequence identity" are relative terms which render said claims indefinite. The specification does not provide an exact standard for ascertaining %identity or %homology, and one skilled in the art would not be reasonably apprised of the scope of the invention. The specification refers to different methods that may be used to measure sequence identity or homology. However, each of these methods may be based on a different mathematical algorithm which could result in inconsistent assessment of sequence identity absent clear recitation of both the algorithm and parameters. Absent the algorithm and parameters employed to determine percent identity of two amino acid sequences, the metes and bounds of the amino acids as instantly claimed cannot be ascertained.

7. Claims 15-22 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite and incomplete for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is ambiguous why the physically and functionally distinct

"N-CAM or L1 isoform" production by "NG108-15 cells *in vitro*" would be any indication for methods for protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal tissue damage in a mammal as claimed. The methods are therefore incomplete for omitting essential steps, in which such omissions amount to a gap between the steps. See MPEP § 2172.01. The omitted steps are when protecting cognitive function, reducing memory dysfunction, treating dementia, and treating a symptom associated with hippocampal tissue damage is completed, as recited in the preambles.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 3-7 and 9-10 are rejected under 35 U.S.C. 102(b) as being anticipated by The Regents of the University of California/Harland et al. (WO 95/06656, 1995 reference; see PTO-892). Harland et al disclose methods of enhancing survival of nerve cells in a mammal, and treatment of conditions characterized by necrosis or loss of neurons, whether central, peripheral or motorneurons (i.e., including the motorneurons affected during spinal cord injury), nerves damaged by traumatic conditions, and the toxic effects of chemotherapeutics (i.e., including mechanical/tumor-induced and chemical injury), and for "therpaeutic applications to treat

congenital conditions or degenerative disorders of the nervous system" through administering the morphogen, dor3, thereby encompassing and meeting all limitations of said claims.

9. Claims 1-10 and 19 are rejected under 35 U.S.C. 102(b) as being anticipated by Wang et al (WO 95/05846, 1995 erference; see PTO-892; see entire reference). Wang et al disclose methods of treating mammal "having a neural defect, neural damage or a neural condition" comprisign adminstering to said mammal "morphogenetic protein"; thus since said disclosure of Wang encompasses all limitations of said claims, i.e. disclosure of Wang et al is drawn to treating mammal with *any* "neural defect, neural damage or a neural condition", said claims are anticipated by the prior art.

Status of Claims

10. No claim is allowed.

11. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology center 1600, Group 1645 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1645 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to John Weatherspoon, Ph.D. whose telephone number is (703) 305-0557.

The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D., can be reached at (703) 308-3995.

John Weatherspoon, Ph.D.

August 26, 1999

Anthony Caputa, Ph.D.

Supervisory Primary Examiner

Group 1645